

Quality of Life and Sexual Function in Patients with Benign Prostatic Hyperplasia

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Incidence of benign prostatic hyperplasia (BPH), one of the most common conditions affecting adult men, increases dramatically after the age of 50. The various symptoms of BPH, which include lower urinary tract symptoms (LUTS), can adversely affect quality of life (QOL). Many men with BPH and LUTS wait until symptoms become significantly bothersome before seeking medical attention. Evaluating the exact severity and significance of symptoms has been difficult with previous methodology. Over the last decade, assessment tools have become available to quantify the symptoms of BPH and LUTS. This article addresses the impact of BPH, its management, and the overall effects it has on QOL. [Rev Urol. 2003;5(2):72-80]

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Benign prostatic hyperplasia (BPH) refers to the excessive cellular growth of the glandular and stromal elements of the prostate. It is one of the most common conditions affecting adult men, with incidence increasing dramatically after the age of 50.¹ The symptoms of BPH, which include difficulty urinating, urgency with leaking or dribbling, and nocturia, can adversely affect sexual functioning and other aspects of quality of life (QOL), but treatment may also compromise QOL by resulting in sexual dysfunction. As a result, many men with BPH and lower urinary tract symptoms (LUTS) wait until those symptoms become significantly bothersome before seeking medical attention.²

Table 1
American Urological Association Symptom Severity Index

Questions to be answered	Circle one number on each line					
	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always
1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5
2. Over the past month, how often have you had to urinate again less than 2 hours after you finished urinating?	0	1	2	3	4	5
3. Over the past month, how often have you found you stopped and started again several times when you urinate?	0	1	2	3	4	5
4. Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5
5. Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5
6. Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5
7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	0 (none)	1 (1 time)	2 (2 times)	3 (3 times)	4 (4 times)	5 (5 times)

Sum of the 7 circled numbers (AUA Symptom Score): _____ Scoring: Mild: 0 to 7 Moderate: 8 to 19 Severe: 20 to 35

The evaluation and management of BPH is complicated by the fact that the normal prostate varies in size and that there is not a clear relationship between the size of the prostate and the severity of the symptoms. Moreover, older methods of evaluation, such as digital rectal examination, are not capable of determining the severity and significance of symptoms. Recently, several tools have been developed to quantify the symptoms of BPH and LUTS. These instruments include the International Prostate Symptom Score (IPSS) and

the American Urological Association (AUA) Symptom Severity Index (Table 1).³

LUTS and Sexual Function

LUTS associated with BPH are often accompanied by sexual dysfunction, including erectile dysfunction (ED) and ejaculatory problems. Interest in sexual intercourse declines with severity of LUTS. Men with more severe LUTS have significantly lower libido, greater difficulty maintaining an erection, and lower levels of sexual satisfaction than men with less severe

LUTS. O'Leary showed that, in men with LUTS, the severity of urinary symptoms appears to exert the greatest influence on the degree of sexual dysfunction.⁴ Burger and colleagues found evidence of a correlation between sexual desire, erectile reliability, and sexual satisfaction and the degree of baseline symptoms.⁵ According to the U.S. National Health and Social Life Survey, both premature ejaculation difficulties and ED are associated with LUTS.⁶ Frankel and colleagues reported that men with storage-related complications

from LUTS, particularly incontinence, had approximately twice the probability of experiencing sexual dysfunction, especially impotence, as men without such complications.⁷ It is unclear whether the sexual dysfunction that occurs with LUTS is due to sleep disturbance, anxiety, or a physiologic effect.⁸ The impact of ED the emotional distress that often accompanies it must be differentiated from LUTS, highlighting the need for several different diagnostic tools when evaluating a patient.⁹

The Multi-national Survey of the Aging Male (MSAM-7) was conducted recently in six European countries and the United States.¹⁰ It included more than 14,000 men of age 50 to 80 years, representing the target population in each country. Overall, 49% reported erection difficulties, 48% had ejaculatory disturbance, and 7% experienced pain during sex. Problems with ejaculation disturbance seem as important as erection difficulty. This survey has clearly confirmed that the extent of the disturbance caused by sexual disorders is strongly related to both age and severity of LUTS. Furthermore, the relationship of sexual disorders affecting QOL to severity of LUTS is independent of age and other comorbidities. This

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relationship confirms the necessity to take sexuality into account in the initial evaluation of a BPH patient and in the choice of the treatment.

Pathophysiology

The pathogenesis of clinical BPH, typified by LUTS, is multifactorial and poorly understood. It includes enlargement of the prostate, the α -adrenergic

mediation of smooth muscle tone in the prostatic capsule and bladder neck, impaired bladder contractility, and bladder instability.¹¹⁻¹³ The prevalence of microscopic, macroscopic, and clinical BPH is age-dependent,¹⁴ and BPH may be a natural result of aging.¹⁵ ED and comorbidities that are directly linked to the development of sexual dysfunction, such as hypertension, diabetes, and certain digestive diseases, are also related to increasing age.¹⁶

Evaluation

History and Laboratory Tests

Urinary symptoms can usually be categorized as obstructive or irritative (Table 2).¹ Notably, these symptoms

Table 2
Clinical Symptoms of Benign Prostatic Hyperplasia

Obstructive	Irritative
Hesitancy	Urinary frequency
Decreased force of stream	Nocturia
Intermittency	Urgency
Incomplete emptying	Dysuria
Terminal dribbling	Urge incontinence
Straining	

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prescribed or over-the-counter medications being taken currently, especially those with anticholinergic or α -adrenergic properties.^{1,3,15} Urinalysis and prostate-specific antigen concentration tests^{3,15} should be included in the workup of any man who presents with LUTS.

QOL Questionnaires

The evaluation should also include an assessment of the impact of symptoms on QOL. The first BPH-specific QOL questionnaire, published in 1988, measured patients' abilities to perform daily activities, levels of BPH-related discomfort, and levels of worry about their health.^{2,17} The authors of the AUA Symptom Severity Index developed additional questionnaires to measure patients' concerns about general health and mental health and the impact of BPH on the patients' QOL.¹⁸

In 1993, Lukacs and colleagues developed a BPH-specific QOL measure consisting of 20 questions related to the physical, mental, social, and general impact of BPH. In 1997, this questionnaire was shortened to nine questions, which is more practical and remains as useful as the original.^{2,19,20} The IPSS, published in 1994, uses virtually the same seven questions as the AUA Symptom Severity Index,

but adds one question concerning the degree to which patients find their symptoms bothersome (ie, “If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?”). This question is now referred to as the “bother score,” although it was previously known as the QOL index.

In 1997, Da Silva and colleagues sought to determine which aspects of QOL were most important to patients and which were most affected by prostatic symptoms. Using an extensive 89-item questionnaire, their team interviewed 117 men. The aspects of QOL deemed most important by patients were sleep, anxiety and worry about their disease, mobility, leisure, daily activities, sexual activities, and satisfaction with sexual relationships. Satisfaction with sexual activities was reported in this and other studies to be most adversely affected by prostatic symptoms.^{2,7,21}

As noted above, the severity of symptoms has been found to have a significant predictive value for sexual dysfunction, and in a study by Puente and colleagues, relation-

Study	Libido, %	Impotence, %	Decreased Ejaculation, %	Ejaculatory Dysfunction, %
VA Study (1996)				
Finasteride	5.0	9.0	NA	2.0
Placebo	1.0	5.0	NA	1.0
PROWESS (1998)				
Finasteride	4.0	6.6	NA	2.1
Placebo	2.8	4.7	NA	0.6
PLESS (1988)				
Finasteride	2.6	5.1	1.5	0.8
Placebo	2.6	5.1	0.5	0.1

VA, Veterans Administration; PROWESS, Proscar Worldwide Efficacy and Safety Study; PLESS, Proscar Long-term Efficacy and Safety Study.
Adapted from Zlotta and Schulman,²⁷ with permission from the publisher, Elsevier Science.

patients with LUTS. However, their reliability varies considerably, making it difficult to base a diagnosis solely on the results of these techniques. However, they can be used in conjunction with digital rectal examination to estimate prostate volume, although prostate size does not have a significant bearing on the degree of

patient's symptoms, his expectations of treatment, and his acceptance of the risks of treatment.

One of the factors most frequently considered by patients contemplating a particular therapy for BPH is the effect of that therapy on sexuality. An inability to ejaculate or a significant decrease in ejaculate volume is significantly associated with deterioration in QOL. The selective α_1 -blockers cause few sexual side effects; as a result, they are associated with a higher QOL. Physicians should inquire about sexual function as part of each patient's pretreatment evaluation and, where appropriate, manage BPH and ED simultaneously.¹⁶

Watchful Waiting

Watchful waiting is usually indicated when symptoms are mild (AUA Symptom Severity Index ≤ 7)³, the patient's QOL is not significantly affected, and treatment offers a lesser benefit. In fact, several studies have found that, with only lifestyle and dietary modifications (eg, decreased fluid intake after dinner and

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ships could be established between the IPSS and ED. In patients with an IPSS greater than 19, which correlates with severe symptoms, there was a clear decrease in sexual function, interest in sexual activity, ability to maintain an erection, and sexual satisfaction.²²

Other Diagnostic Tests and Procedures

Other diagnostic tests (quantitative measures), such as uroflowmetry and cystourethroscopy, have been used in

obstruction or symptoms. Postvoid residual volume also has a high degree of intrinsic variability, which limits the value of this test.²³

Treatment Options for Symptomatic BPH

Symptoms related to BPH, particularly LUTS, can be managed by waiting for spontaneous improvement of symptoms, by medical therapies, or by various surgical procedures. The choice of treatment depends on the severity and annoyance of the

a moderated or lessened consumption of alcoholic and caffeinated beverages), 32%–42% of patients report decreased symptom severity, 26%–51% report no change in symptoms, and only 16%–32% report symptom worsening.^{2,11}

Medical Management

Medical management may be indicated when symptoms are moderate (AUA Symptom Severity Index 8–19) or LUTS are sufficiently bothersome to warrant intervention. Choices for medical management include 5- α -reductase inhibitors, α_1 -blockers, and phytotherapy.³

5- α -Reductase inhibitors. Finasteride is the only 5- α -reductase inhibitor approved by the U.S. Food and Drug Administration (FDA) for the treatment of patients with LUTS suggestive of BPH.¹⁵ Finasteride decreases the conversion of testosterone to dihydrotestosterone, leading to a reduction in prostate size and improving urinary flow and symptoms.²⁴ However, studies suggest that this effect may take from 3 months to as long as 12 months after the initiation of therapy to fully manifest itself.¹⁵ Finasteride has been found effective and safe in both older and

in patients with moderate or severe symptoms, treatment with finasteride 5 mg once daily reduced the risk of progression to acute urinary retention (AUR) or transurethral resection of the prostate (TURP) by 50% over a 4-year period.²⁶ Commonly reported side effects of finasteride include decreased libido, ED, and ejaculatory dysfunction.³ The findings of three studies examining the occurrence of these side effects are summarized in Table 3.²⁷ Notably, finasteride has been associated with a greater incidence of impotence than have α_1 -blockers.^{28,29}

α_1 -Blockers. All of the currently available α_1 -blockers have demonstrated efficacy in treating symptoms of BPH. Some of these agents, such as terazosin and doxazosin, were originally developed for the treatment of hypertension; newer uroselective α -blockers, such as tamsulosin and alfuzosin OD (currently under evaluation by the FDA), are designed specifically to manage the clinical symptoms of BPH (Table 4).²⁸

Selective α_1 -blockers are currently considered the standard of care³⁰ and the most effective medical therapy for LUTS suggestive of BPH³¹ because of their efficacy, specificity for the

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younger men,²⁵ although a small number of patients demonstrate no response. Response has been correlated with prostate size before treatment; men with prostates weighing more than 40 g appear to respond more favorably than men with smaller prostates.^{2,3}

Long-term beneficial effects have been demonstrated with finasteride. The Finasteride Long-Term Efficacy and Safety Study demonstrated that,

urinary tract, limited side effects, simplicity of dosing, and rapid onset of action. Their use is based on the presence of contractile tissue in the prostate mediated via α_1 -adrenergic receptors abundant in the bladder neck, prostate capsule, and stroma. This dynamic component contributes to approximately 40% of outflow obstruction.^{32,33}

Selective α_1 -blockers such as prazosin, terazosin, and doxazosin are

Table 4
Currently Available α_1 -Blockers

Nonselective α_1 -Blockers

- Phenoxybenzamine

Selective α_1 -Blockers

- Prazosin
- Alfuzosin IR

Selective Long-Acting α_1 -Blockers

- Terazosin
- Doxazosin
- Tamsulosin
- Alfuzosin SR
- Alfuzosin OD (under FDA review)

IR, immediate release; SR, sustained release; OD, once daily; FDA, U.S. Food and Drug Administration.

Adapted from Downs and O'Leary,²⁸ with permission from the publisher, Lippincott Williams and Wilkins.

usually administered at bedtime and titrated up to the desired dose over 5–10 days. Although they were originally developed as antihypertensives, these agents result in mean blood pressure changes of only 1–4 mm Hg in normotensive patients, whereas hypertensive patients may see reductions of 10–15 mm Hg.¹⁵ A study by Lepor and colleagues in 1992 showed that terazosin improved symptom scores and peak urinary flow rates in patients with LUTS.³⁴ The most common side effects were asthenia, postural hypotension, and dizziness, which occurred in 5%–10% of patients. Based on these effects, it is important to consider the morbidity associated with falls when this drug is used in the elderly.¹⁵

Several large meta-analyses have reviewed the efficacy of selective α_1 -blockers in the treatment of LUTS suggestive of BPH. Heimbach and Müller,³⁵ Chapple,³⁶ and Djavan and Marberger³⁷ concluded that overall improvement in symptom scores and increases in maximum urine flow

rate did not vary significantly among agents (Table 5).³⁰ Although these different agents may have similar efficacy, they vary in their uroselectivity, which is a highly relevant consideration in the management of BPH,³⁰ particularly as it relates to side effects.^{30,31} Additionally, there are differences in their effects on sexual function (Table 6).³⁰

The safety profile of α_1 -blockers that act preferentially on the lower urinary tract, such as alfuzosin and tamsulosin, is favorable.²⁹ The incidence and severity of cardiovascular side effects are reduced in comparison with other α_1 -blockers. In clinical trials, treatment with alfuzosin and tamsulosin resulted in fewer patient discontinuations due to adverse effects such as orthostatic hypotension and dizziness than has treatment with doxazosin, terazosin, and prazosin.³⁰

Abrams and colleagues reported improvements in symptoms and urinary flow rates after 4 weeks of therapy in patients receiving tamsulosin, with a mean response rate of 67% across the study population.³⁸ In a meta-analysis, Chapple and colleagues reported a decrease of at least 25% in symptom scores among 66% of patients who received tamsulosin and among 49% of controls.³⁹ Tamsulosin did not alter standing or supine blood pressure or pulse rates, and the overall incidence of adverse events, such as headache, dizziness, and infection, was comparable to

Independent of their effects on LUTS, α_1 -antagonists may produce a beneficial effect on sexual function.

that of placebo. Additionally, rhinitis was observed in 13.1% of the patients who received a lower dose of tamsulosin (0.4 mg) and 17.9% of the patients who received a higher dose (0.8 mg).⁴⁰ This unexpected side

Agent	Change from Baseline in TSS, %	Change from Baseline in Q_{max} , mL/s
Alfuzosin SR	-31	+2.4 (29%)
Terazosin	-38	+2.2 (23%)
Doxazosin	-17	+2.3
Tamsulosin	-36	+1.4 (13%)

TSS, indicates total symptom score; Q_{max} , peak flow rate; and SR, sustained release.
Adapted from Debruyne,³⁰ with permission from the publisher, Elsevier Inc.

Agent	Impotence, %	Ejaculation Failure, %	Decreased Libido, %
Alfuzosin SR	2.2	0.0	0.6
Terazosin	6.0	0.3	3.0
Tamsulosin	0.8	4.5	1.0

SR, sustained release.
Adapted from Debruyne,³⁰ with permission from the publisher, Elsevier Inc.

effect may be a significant nuisance for patients; however, many physicians and patients may not realize the direct relationship between this adverse event and treatment.

Alpha₁-antagonists may enhance erectile function by decreasing sympathetic tone in the penis, leading to

colleagues reported a progressive improvement in patients' self-reported health-related QOL status (30%, 37%, and 43% improvement from baseline at 3, 6, and 12 months, respectively) after treatment with alfuzosin. Patients' perceived sexual satisfaction also improved significantly from baseline, with degree of improvement correlating with age.⁴² Overall, middle-aged patients with moderate to severe symptoms at baseline benefited most from treatment with alfuzosin.

In an open-label tamsulosin study, 30% of subjects reported abnormal ejaculation and 6% reported impotence.⁴⁴ Overall, alfuzosin SR had the lowest reported incidence of undesirable sexual side effects, including impotence, abnormal ejaculation,

and decreased libido, when compared with terazosin and tamsulosin.³⁰

Phytotherapy. In the United States, phytotherapy is widely used for the management of LUTS suggestive of BPH. Its use in Europe is even more common.^{1,45} However, few thorough scientific studies of medicinal botanicals have been conducted because of difficulties such as a lack of standardized preparations.³²

Beta-sitosterol is believed to be the active component in many of the botanicals used to manage LUTS. The two most frequently used botanicals are extracts from the saw palmetto berry and African plum tree bark. Both have shown improvement in urinary symptoms and urinary flow rates comparable to that achieved with finasteride, but without any readily apparent adverse effects.¹ A study by Berges and colleagues showed a significant improvement in symptoms and urinary flow parameters in subjects receiving β -sitosterol 20 mg three times per day.⁴⁶ The mechanism of action of β -sitosterol is still unknown.

It is believed that phytotherapy will continue to be used extensively by patients throughout the world. As a result, it is recommended that physicians become familiar with these agents and act as advocates for standardized preparations and more clinical studies assessing their safety and efficacy.¹

Surgical Intervention

Patients with an AUA Symptom Severity Index of 20 to 35 may initially be managed medically. If the patient fails medical management, surgery must be considered.³ Indications for surgery include AUR, azotemia, recurrent urinary tract infections, bladder calculi, obstructive uropathy, hydronephrosis, renal insufficiency, overflow incontinence, and severe recurrent hematuria related to

venous dilatation of the prostate.^{1,3}

Transurethral resection of the prostate. TURP is the mainstay of surgical treatment for BPH and remains the gold standard against which other treatments for BPH are measured. One study reported a 70%–85% improvement in AUA Symptom Severity Index in 80%–90% of cases.¹ In contrast to finasteride, TURP appears most suc-

cessful in patients whose prostates weigh less than 40 g.³ Morbidity has been decreasing in recent years but still approaches 25%.¹

Indications for surgery include AUR, azotemia, recurrent urinary tract infections, bladder calculi, obstructive uropathy, hydronephrosis, renal insufficiency, overflow incontinence, and severe recurrent hematuria related to venous dilatation of the prostate.

Possible postoperative complications affecting sexual function include retrograde ejaculation (occurring in approximately one third of patients), impotence or ED not present preoperatively (which can occur in 10%–15% of patients), and incontinence.^{15,47,48} In addition, common, immediate postoperative complications include hyponatremia, urinary incontinence, stricture, urinary tract infection, and need for blood transfusion.³

Open prostatectomy. Open prostatectomy is usually reserved for patients with large prostates (ie, weighing 60–80 g) or comorbidities such as large bladder diverticula or large bladder stones.³ Outcomes and complications are similar to those for TURP.¹

Minimally invasive treatments. A variety of minimally invasive treatments has been introduced in recent years. Many of these treatments result in shorter hospital stays or outpatient management and fewer risks of postoperative complications than does TURP. However, the long-

term efficacy, safety, and cost-effectiveness of these procedures are still unclear.¹¹

One such procedure is transurethral incision of the prostate (TUIP), which was developed, studied, and initially promoted by Orandi in the 1970s. This minimally invasive endoscopic procedure favors patients with prostates weighing less than 30 g. As with TURP, 80%–90% of patients demonstrate improved symptoms. However, operating time is shorter, and less blood loss and fewer postoperative complications result. In one study, retrograde ejaculation occurred in only 13% of patients undergoing TUIP compared with 37% undergoing TURP.¹⁵ Thus, TUIP, which has been called an underused procedure with which the newer, less invasive treatments should be compared,⁴⁹ appears to be the procedure of choice for men in whom fertility and the ability to ejaculate are important.¹¹

Another minimally invasive technique is transurethral microwave thermal therapy (TUMT). One comparison study has shown it to be somewhat less effective than TURP, with improvement in symptoms and peak urinary flow rates, respectively, demonstrated in 68% and 69% of TUMT patients and in 78% and 100% of TURP patients.⁵⁰ However, a study by Francisca and colleagues showed that TUMT preserved postoperative sexual function, particularly the ability to sustain an erection and the ability to ejaculate, to a greater degree than did TURP.⁵¹

Transurethral needle ablation (TUNA) delivers low radiofrequency

energy directly into selected areas of the prostate, producing coagulation necrosis while sparing the urethral mucosa. Its effectiveness has been demonstrated in several studies.⁵²

Summary

There is a high prevalence of BPH and LUTS in the aging male population.²⁸ Manifestations exhibit considerable variation in onset and progression. Pathophysiology is multifactorial and not completely understood.¹⁴ Medical treatment can reduce symptom severity and improve QOL for most patients. Patients with severe symp-

Studies have shown a clear relationship between LUTS suggestive of BPH and ED, and an increased severity of urinary symptoms is associated with higher rates of sexual dissatisfaction.^{5,7,16,29,53,54} The patient with BPH should routinely be asked about sexual dysfunction as part of the pretreatment evaluation.²⁸ When it is discovered as a comorbidity, it should be managed conservatively at the same time as the BPH.¹⁶

For patients with moderate symptoms, α_1 -blockers present a rational first-line therapy, having been shown to reduce symptom scores safely and

to AUR or the need for surgery.^{24,55}

Patient decisions regarding treatment choices are based more on anticipated relief of symptoms and improved QOL than on traditional measures of urinary symptoms, such as peak urinary flow rates.⁵⁶ Improving sexuality-related QOL is an important outcome for patients. This underscores the importance of measuring sexual function before and after treatment.²⁸ Hopefully, the medical community will soon agree on standardized, validated measures that will allow for comparative analysis.² ■

Among the α_1 -blockers used to manage BPH, the uroselective agent alfuzosin has demonstrated the lowest incidence of sexual side effects.

toms may require surgery.¹¹ Many patients will try phytotherapy, which frequently includes saw palmetto berry and African plum tree extracts.¹

There are several methods of assessing symptom severity in patients with BPH; the IPSS and AUA Symptom Severity Index are the best known.⁴ Other methods have been developed to assess the impact of urinary symptoms on QOL. However, many of these methods are in development, and there is no agreement on standardization.²

effectively, increase urinary flow rates, and improve QOL.² Although they are similarly efficacious, these agents differ in their clinical uroselectivity and side-effect profiles.³⁰ Among the α_1 -blockers used to manage BPH, the uroselective agent alfuzosin has demonstrated the lowest incidence of sexual side effects. In patients with prostates that weigh more than 40 g, the 5- α -reductase inhibitor finasteride has demonstrated long-term potential to reduce gland size and block progression of the disease

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Main Points

- Benign prostatic hyperplasia (BPH) and its associated lower urinary tract symptoms (LUTS) are highly prevalent in the aging male population.
- Both LUTS and their treatment can adversely affect sexual functioning and other aspects of quality of life (QOL).
- Pretreatment evaluation of patients with LUTS suggestive of BPH should include an assessment of sexual functioning; when sexual dysfunction is discovered, it should be treated at the same time as the BPH.
- Treatment options for symptomatic BPH include watchful waiting, medication management, and surgery.
- Medication management is usually indicated when symptoms are moderate or sufficiently bothersome to warrant intervention; medication can reduce symptom severity and improve QOL for most patients.
- Patients with severe symptoms may initially be managed medically, but if medical treatment fails, surgery must be considered.

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